ARTIGO DE REVISÃO

PATOFISIOLOGIA DA DOR ONCOLÓGICA: REVISÃO DE LITERATURA

PATHOPHYSIOLOGY OF ONCOLOGICAL PAIN: REVIEW OF LITERATURE

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RESUMO

Apesar dos insumos à diagnose e terapêutica do câncer, a doença continua trazendo agravo à qualidade de vida dos enfermos, sendo a dor referida como queixa frequente, com prevalência variando entre 50 e 53% em pacientes com câncer em todos os estágios, e até 70% nos casos de doença avançada. A dor oncológica se manifesta conforme a localização primária do câncer, metástase, acometimento ósseo, proximidade com sistema nervoso, produção de substâncias químicas promotoras da dor, e fatores relacionados ao paciente como ansiedade e depressão. Por ser subjetiva, não palpável, e uma experiência individual e de difícil avaliação, requer para a equipe de saúde suporte educacional, conhecimento e instrumentos que contribuam para a sua compreensão, sendo a elucidação de seus mecanismos biológicos objeto desta revisão de literatura.

Palavras-chave: Dor Oncológica. Dor. Cuidados Paliativos. Fisiologia da dor.

ABSTRACT

Despite the contributions to the diagnosis and treatment of cancer, the disease continues to present an adverse effect on patients' quality of life, with pain being a frequent complaint, with a prevalence varying from 50 to 53% in cancer patients at all stages and up to 70 % in cases of advanced disease. Cancer pain is manifested by the primary site of cancer, metastasis, bone involvement, proximity to the nervous system, production of pain-promoting chemicals, and patient-related factors such as anxiety and depression. Because it is subjective, not palpable, and an individual experience and difficult to evaluate, requires for the health team educational support, knowledge and instruments that contribute to their understanding, being the elucidation of its biological mechanisms object of this literature review.

Keywords: Oncologic Pain. Pain. Paliative Care. Physiology of pain.

ACESSO LIVRE

Citação: Schmidt LYS, Castro AFO, Siqueira JGL, Oliveira DP, Assis WRF (2020) Pathophysiology of oncological pain: review of literature. Revista de Patologia do Tocantins, 7(1):.59-61

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Editor: Guedes V. R. Medicina, Universidade Federal do Tocantins, Brasil.

Publicado: 28 de junho de 2020.

Conflito de interesses: os autores declararam que não existem conflitos de interesses.

INTRODUCTION

Despite the inputs to the diagnosis and treatment of cancer, the disease continues to affect the quality of life of the population, and pain is reported as a frequent complaint, affecting approximately 50% of the patients in all stages of the disease and around 70% of the patients cases of advanced disease[1,7].

The oncologic pain is manifested due to the growth of the primary tumor or its metastases, to the research methods and even as an effect of the usual treatment therapies, such as chemotherapy and radiotherapy[2]. Its management should be prioritized through the impact on physical activity, appetite, sleep, mood and quality of life of the individual in the process of coping with the disease, reflecting on psychic suffering, questions of a metaphysical nature and aggravation of endocrine-immunological parameters[3,7].

According to the World Health Organization (WHO) estimate, of the 5 million people who die of cancer each year, 4 million die from uncontrolled pain, and most cases are effectively attenuated by pharmacological interventions and mental relaxation techniques.[4]

Cancer pain relief involves a global intervention that considers the physical, social, psychological, emotional, and spiritual aspects of suffering, called palliative treatment. The palliative treatment integrates a therapeutic plan for the patient who does not respond to the curative treatment, aiming to promote quality of life and well-being to this and their relatives in the psychosocial-emotional-biological environments - it also implements the curative treatment of cancer in its earliest stages. [5,12]

The pain symptom is an unpleasant sensory and emotional experience with intensity proportional to the disease progression, varying according to the primary location of the cancer, metastasis, bone involvement, proximity to the nervous system, production of pain-promoting chemicals, and factors related to the patient as anxiety and depression. In addition, pain intensity is the preponderant factor to predict the need for pain relief.[12]

According to the International Society for the Study of Pain, pain is "an unpleasant sensory and emotional experience, which is described in terms of actual or potential tissue damage. Pain is always subjective and each individual learns to use."[5] Because it involves diverse and complex aspects, the management of cancer pain requires the evaluation and treatment of the physical, emotional, social and spiritual components[5,12], being the biological dimension the purpose of this article.

METHODOLOGY

The information contained in this study was obtained by bibliographic survey of specialized literature present in books, guidelines, consensuses and periodicals in the English and Portuguese language published on the free access platforms PubMed and LILACS (Latin American and Caribbean Literature in Health Sciences), using the descriptors Oncologic Pain, Pain, Palliative Care and Physiology of Pain. It wasobtained a sample of 13 publications, useful to the discussion of the developed theme.

RESULTS AND DISCUSSION

Epidemiology

It is estimated that in 2012 there were 14.1 million new cases of cancer and 8.2 million deaths due to this cause in the world, according to the conclusion of the V revision of GLOBOCAN. Lung cancer ranks first in incidence, and mortality, followed respectively by breast, colorectal, prostate, stomach and liver, accounting for 55% of the overall incidence this year. As of 2025, more than 20 million new cases of cancer are expected annually, especially in developing and undeveloped countries[7,13].

Pathophysiology

The primary neurons of the pain pathway, called sensory afferent neurons, innervate the skin and almost all of the internal organs. They are the gateway to the transmission of sensory information from peripheral tissues to the medulla and brain, capable of detecting varieties of stimulus types, encompassing those of a physical and/or chemical nature through their different receptors and transduction molecules[5,8].

The cell bodies of the sensory fibers that innervate the head and body are located in the trigeminal ganglion and dorsal root ganglia, respectively, and fall into two main categories: larger diameter myelinated A fibers and unmyelinated C fibers , of smaller diameter. Most myelinated A-beta fibers carry non-harmful stimuli applied to the skin, joints and muscles. In addition, a large part of the myelinated non-myelinated C-sensory and A-delta sensory fibers are specialized and called nociceptors. These have the function of identifying and converting environmental stimuli - thermal, mechanical, chemical - harmful, into electrochemical signals transmitted to the central nervous system[5,8].

In order to detect noxious stimuli, nociceptors express a complex set of receptors that are activated by proinflammatory factors released by damaged tissue, are these protons, endothelin, prostaglandin, bradykinin and neural growth factor. Vanyloid (VR1) receptors, expressed by most nociceptors, detect heat, acid, extracellular protons and lipid metabolites. To detect harmful mechanical stimuli, they activate signaling cascade in response to excessive stretching and ATP-activated receptors[8].

The plasticity of sensory neurons allows the change of their phenotype in response to a sustained peripheral lesion that alters peptide-signaling patterns and expression of tissue growth factors.This change depends, in part, on peripheral sensitization, in which the level of activation of the nociceptor threshold is reduced, so that what would normally be perceived as a mild noxious stimulus is perceived as highly harmful - hyperalgesia - or stimuli that normally would be perceived as non-harmful are perceived as harmful - allodynia. Peripheral tissue damage has also been shown to previously activate "silent" or "dormant" nociceptors, making them highly responsive to normally non-harmful or slightly harmful stimuli[5,6,8].

Research has shown that peripheral sensitization of nociceptors is closely involved in the origin and maintenance of pain associated with bone cancer[5].

A tumor is made up of cancerous cells and other types, such as cells of the immune system constituting macrophages, neutrophils and T cells, which secrete direct or excitatory sensitizing factors from primary afferent neurons, including prostaglandins, tumor necrosis factor alpha, endothelin, growth factor vascular endothelial (VEGF), interleukin 1 and 6, tissue growth factor, platelet derived growth factor. Tumors are not predominantly innervated by sensory neurons, however growth and proteolytic enzymes damage the nerves by compression and by direct proteolysis, respectively, resulting in neuropathic pain[6,8].

The transmission of the sensory stimulus to the spinal cord neurons of the spinal cord ascends through the spinothalamic tract to the CNS and through different parallel neuronal pathways, which explains the pain being described predominantly of high intensity. The amygdala and the cerebral cortex can modulate the ascending conduction of pain, justifying the influence of the patient's mood and attitude in determining the degree and degree of pain[5,8].

Irruptive pain is characterized by a transient accentuation of previously moderate pain intensity, despite the administration of analgesic therapy, which may be intermittent, related or not to movement, indicative of inadequate management of analgesic therapy. 64 to 90% of patients with cancer pain experience this type. In most cases the etiology is primarily neoplastic (76%) or secondary to treatment (20%). Some factors are related to the precipitation of the seizures, they are movement, ambulation, coughing, orthostatism, intestinal constipation, urinary infection and regurgitation of the medication. About 33%, 27%, 20% and 20% of the irruptive pains are somatic, neuropathic, visceral and mixed, respectively[9].

CONCLUSION

The management of pain in cancer patients aims at the overall rehabilitation of the individual in a biopsychosocial perspective, and the biological understanding of pain by the health professional is a basic component of care planning[4].

Because it is subjective, not palpable, and an individual experience and difficult to evaluate, it requires the health team to provide educational support, knowledge and instruments that contribute to their comprehension[5], which ends up reducing or eliminating the use of inadequate analgesic regimes, underestimation of pain and the dissemination of misconceptions about cancer pain.

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